IN THE CLAIMS:

This listing of claims will replace all prior versions and listings of claims in the application:

In the Claims:

Please replace the claims with the following listings of claims:

1. (Canceled).

2. (Canceled).

3. (Currently Amended) ~~A method according to claim 2, wherein the algorithm performs the following steps:~~ A method for quantitating the individual contribution of a mutation or combination of mutations to a drug resistance phenotype exhibited by HIV, said method comprising the step of

a) performing a linear regression analysis using data from a dataset of matching genotypes and phenotypes,

wherein the log fold resistance, pFR, of each HIV strain is modelled as the sum of all the individual resistance contributions for each of said mutations or combinations of mutations that occur in HIV according to the following equation:

$$pFR = \beta_A M_A + \beta_B M_B + \beta_n M_n + \cdots + \beta_Z M_Z + \varepsilon$$

wherein each individual resistance contribution is calculated by multiplying a mutation factor, M_A, M_B, ... M_Z, for each of said mutation or combination of mutations by a resistance coefficient β_A, β_B, ... β_Z;

wherein for a combination of mutations, the mutation factor M_n represents the co-occurrence of one mutation with other one or more mutations and a coefficient β_n represents the synergy or antagonism between the one mutation with the other one or more mutations;

wherein the mutation factor assigned to each of said mutation or combination of mutations reflects the degree to which said mutation or combination of mutations is present in the HIV strain and, if present, to which degree said mutation is present in a mixture;

wherein each resistance coefficient reflects the contribution of said mutation or combination of mutations to the fold resistance exhibited by the strain;

wherein the error term ε represents the difference between a modelled prediction and an experimentally determined measurement;

b) removing mutations that do not contribute to said drug resistance phenotype by tracking the change in pFR as the effects of each of said mutation or combination of mutations are removed from said dataset, further comprising:

~~a)~~i) ~~calculate~~calculating average pFR for all mutations with a sufficient count in the database to be significant;

~~b)~~ii) ~~determine~~determining ~~the extremes (~~maximum~~,~~ extreme and minimum~~)~~ extreme, and select ~~the~~ mutation with the pFR furthest away from ~~the~~a global average;

~~c)~~iii) ~~remove~~removing all virus strains that have ~~the~~said selected mutation from ~~the~~said dataset and ~~reiterate~~reiterating ~~from~~ steps ~~a~~i) to iii);

d. stop when ~~the~~ said selected mutation in step ~~b~~ ii) has an average pFR that approximates to ~~the~~ said global average; wherein said average pFR is within a fraction of standard deviation of the remaining mutations;

such that removing virus strains with a certain resistance causing mutation results in an increase of the average pFR for correlating mutations, which thus have a higher average pFR;

thereby quantitating the individual contribution of said mutation or combination of mutations to a drug resistance phenotype exhibited by HIV.

4. (Currently Amended) A method ~~according to claim 1~~ for quantitating individual contribution of a mutation or combination of mutations to a drug resistance phenotype exhibited by HIV, comprising the step of

a) performing a linear regression analysis using data from a dataset of matching genotypes and phenotypes.

wherein the log fold resistance, pFR, of each HIV strain is modelled as the sum of all individual resistance contributions for each of said mutations or combination of mutations in HIV according to the following equation:

$$pFR = \beta_A M_A + \beta_B M_B + \beta_n M_n + \cdots + \beta_Z M_Z + \varepsilon$$

wherein said all individual resistance contribution is calculated by multiplying a mutation factor, M_A , M_B , ... M_Z, for each mutation or combination of mutations by a resistance coefficient β_A, β_B, ... β_Z;

wherein for a combination of mutations, the mutation factor M_n represents the co-occurrence of one mutation with other one or more mutations and the coefficient β_n represents the synergy or antagonism between the one mutation with the other one or more mutations;

wherein the mutation factor assigned to each of said mutation or combination of mutations reflects the degree to which that mutation or combination of mutations is present in said HIV strain and, if present, to which degree the mutation is present in a mixture;

wherein each resistance coefficient reflects the contribution of said mutation or combination of mutations to the fold resistance exhibited by said HIV strain;

wherein the error term ε_i represents the difference between a modelled prediction and an experimentally determined measurement, further comprising~~, wherein the algorithm performs the following steps~~:

~~a)~~b) ~~calculate~~calculating correlation coefficient between all mutations with a sufficient count in the database and the pFR;

~~b)~~c) ~~determine~~determining ~~the extremes (maximum, minimum)~~ maximum extreme and minimum extreme, and ~~select~~selecting ~~the~~ mutation with the highest absolute value of correlation coefficient;

~~c)~~d) ~~calculate~~calculating a linear model for the pFR with ~~the~~ said selected mutation(s) ~~(~~from step c~~b), all previous iterations)~~;

~~d)~~e) ~~take~~taking ~~the~~a residue, wherein said residue is pFR minus said modeled prediction;

~~e)~~f) ~~calculate~~calculating correlation coefficient between all mutations with a sufficient count in ~~the~~said database and ~~the~~said residue;

~~f)~~g) ~~determine~~determining ~~the extremes (maximum, minimum)~~a maximum extreme and a minimum extreme, and ~~select~~selecting ~~the~~ mutation with the highest absolute value of correlation coefficient;

~~g)~~h) ~~calculate~~calculating a linear model for the pFR with ~~the~~ said selected mutation(s) ~~(~~from step g~~f), all previous iterations)~~; and

~~h)~~i) ~~reiterate~~reiterating ~~from step~~steps c~~d)~~ to g);

~~i)~~stop when ~~the~~said selected mutation in step hg) has a correlation coefficient that approximates to zero;~~.~~

thereby quantitating the individual contribution of said mutation or combination of mutations to a drug resistance phenotype exhibited by HIV.

5. (Canceled).

6. (Currently Amended) A method ~~according to claim 5~~ for quantitating the individual contribution of a mutation or combination of mutations to a drug resistance phenotype exhibited by HIV, said method comprising the step of:

a) performing a linear regression analysis using data from a dataset of matching genotypes and phenotypes, wherein the log fold resistance, pFR, of each HIV strain is modelled as the sum of all the individual resistance contributions for each of said mutations or combinations of mutations that occur in HIV according to the following equation:

$$pFR = \beta_A M_A + \beta_B M_B + \beta_n M_n + \cdots + \beta_Z M_Z + \varepsilon$$

wherein each individual resistance contribution is calculated by multiplying a mutation factor, M_A, M_B, ... M_Z, for each of said mutation or combination of mutations by a resistance coefficient β_A, β_B, ..., β_Z;

wherein for a combination of mutations, the mutation factor M_n represents the co-occurrence of one mutation with other one or more mutations and the coefficient β_n represents the synergy or antagonism between the one mutation with the other one or more mutations;

wherein the mutation factor assigned to each mutation or combination of mutations reflects the degree to which said mutation or combination of mutations is present in said HIV strain and, if present, to which degree the mutation is present in a mixture;

wherein each resistance coefficient reflects the contribution of the mutation or combination of mutations to the fold resistance exhibited by said strain;

wherein the error term ε, represents the difference between a modelled prediction and an experimentally determined measurement;

wherein censored values in said genotype / phenotype database are replaced by a maximum likelihood estimation;

wherein for each iteration of the linear regression, the following steps are performed until the predictions converge:

a) ~~Calculate~~calculating a linear regression model without censored values;

b) ~~Use~~using ~~the~~a phenotypic measured value V_0 as if the censor was " = ", ~~e.g.~~ when a result is expressed as $-\log FR < 4$, ~~we will treat~~ V_0 is treated as $-\log FR = 4$;

c) ~~Look~~looking at the prediction P from the model and apply either:

When case '<'-censor:

~~-~~i) $P < V_0 - 0.798\ \sigma$ (center of gravity of half Gaussian distribution)

~~o~~ Remove value from training data for the next iteration

~~-~~ii) $V_0 - 0.798\ \sigma \leq P < V_0$

~~o~~ Use $V' = V_0 - 0.798\ \sigma$ for the next iteration

~~-~~iii) $V_0 \leq P$

~~o~~ Use V' centre of gravity of tail (<V) of a normal distribution N (P, σ) as value for the next iteration.

When case '>'-censor:

~~-~~i) $P > V_0 + 0.798\ \sigma$ (center of gravity of half Gaussian distribution)

~~o~~ Remove value from training data for the next iteration

~~-~~ii) $V_0 + 0.798\ \sigma \geq P > V_0$

~~o~~ Use $V' = V_0 - 0.798\ \sigma$ for the next iteration

~~-~~iii) $V_0 \geq P$

~~o~~ Use V' centre of gravity of tail (>V) of a normal distribution N (P, σ) as value for the next iteration.;

d) ~~Calculate~~calculating a linear regression model and for the censored values in the linear regression model, either remove the data-point from the training set, or use V' instead of the censored phenotypes measurement, as described in step c);

e) ~~Re-iterate~~reiterating from step b) until the prediction converges;

thereby quantitating the individual contribution of said mutation or combination of mutations to a drug resistance phenotype exhibited by HIV.

7. (Canceled).

8. (Currently Amended) ~~A~~The method according to claim ~~1~~3, wherein the contribution of a mutation pattern to the drug resistance phenotype exhibited by an HIV strain is calculated, said method comprising the steps of:

a) obtaining a genetic sequence of said HIV strain,

b) identifying the pattern of mutations in said genetic sequence, wherein said mutations are associated with resistance or susceptibility to drug therapy, and

c) calculating the fold resistance of the HIV strain as compared to the wild type HIV strain by performing a linear regression analysis according to claim 1.

9. (Canceled).

10. (Currently Amended) ~~A~~The method according to claim ~~1~~3, wherein in the case of small datasets for particular mutations or combinations of mutations, the method is applied recursively to the set of virus strains that exhibit those particular mutations or combinations of mutations.

11. to 13. (Canceled).

14. (Currently Amended) A diagnostic system for quantitating the individual contribution of a mutation or combination of mutations to the drug resistance phenotype exhibited by an HIV strain, said system comprising:

a) means for obtaining a genetic sequence of said HIV strain;

b) means for identifying the mutation pattern in said genetic sequence as compared to wild type HIV;

c) means for predicting the fold resistance exhibited by the HIV strain using the method of claim ~~1~~3.

15. (Currently Amended) A computer apparatus or computer-based system adapted to perform the method of claim ~~1~~3.

16. (Currently Amended) A computer program product for use in conjunction with a computer, said computer program product comprising a computer readable storage medium and a computer program mechanism embedded therein, the computer program mechanism comprising a module that is configured so that upon receiving a request to quantify the individual contribution of a mutation or combination of mutations to the drug resistance

phenotype exhibited by HIV, or to calculate the quantitative contribution of a mutation pattern to the drug resistance phenotype exhibited by an HIV strain, it performs a method according to claim ~~1~~3.